IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of: Clifford J. Herman
Art Unit: 1617
Serial No.: 10/554,133
Filed: October 20, 2005
Confirmation No.: 9352
For: METHYLPHENIDATE SOLUTION AND ASSOCIATED METHODS OF ADMINISTRATION AND PRODUCTION
Examiner: Deirdre Renee Claytor

February 5, 2008

Declaration of Inventor Clifford J. Herman

I, Clifford J. Herman, declare as follows:

1. I am the sole inventor of the subject matter claimed in the above-entitled United States patent application, Serial Number 10/554,133.

2. I have reviewed the final Office action issued November 13, 2007 in this application, and the Midha et al. (U.S. Patent No. 6,127,385) and Epstein et al. (U.S. Patent Application Publication No. 2002/0103162) references cited therein. I have reviewed all pending claims of this application, including claims 1-23.

3. The present invention is directed to a storage stable methylphenidate solution (e.g., a solution of the free base or a pharmaceutically acceptable salt thereof) that has improved chemical stability, and therefore improved storage stability or shelf-life as well. As noted in the present application, I have discovered that by preparing a solution of methylphenidate using a solvent system comprising a combination of water and a non-aqueous solvent, and in particular, a solvent system comprising less than about 50% water (or alternatively greater than about 50% of the non-aqueous solvent), the chemical stability, and therefore the storage stability or shelf-life, of the solution is improved.

4. The Midha et al. reference discloses a method of treating depression in a patient by oral or non-oral administration of the active 1-threo-methylphenidate, which may be in the form of the free base or a pharmaceutically acceptable salt. (See, e.g., column 1, lines 5-8, and column 2, lines 36-38). Further, Midha et al. make a general reference to a solution containing the active, ascorbic acid, and an aqueous or non-aqueous solvent (see, e.g., column 4, lines 59-63).

5. The Epstein et al. reference discloses methods and compositions for enhancing long-term memory function and/or performance. (See, e.g., paragraph [0006].) Further, Epstein et al. make a general reference to the preparation of a solution of a methylphenidate compound using, among other things, water, a polyol or a mixture thereof (see, e.g., paragraph [0250]) as a solvent.

6. Neither Midha et al. nor Epstein et al., alone or in combination, disclose or suggest a storage stable solution comprising methylphenidate, or methylphenidate HCl, and a solvent system that has a water concentration of less than 50%. More specifically, the combination of Midha et al. and Epstein et al. fail to disclose a storage stable solution comprising such a solvent system, wherein:

(i) the water concentration is between about 10% and about 45% and the non-aqueous solvent concentration is at least about 50% (Claim 1);

(ii) the water concentration is less than about 50%, the polyol concentration is between about 30% and about 70%, and the glycol concentration is between about 10% and about 70% (Claim 9);

(iii) the water concentration is between about 10% and about 45%, the polyol concentration is between about 40% and about 60%, and the glycol concentration is between about 10% and about 30% (Claim 14); or,

(iv) the water concentration is between about 30% and about 40%, the polyol concentration is between about 45% and about 55%, and the glycol concentration is between about 10% and about 20% (Claim 19).

7. Furthermore, neither Midha et al. nor Epstein et al. recognize or acknowledge that methylphenidate solutions are inherently unstable. As a result, neither of the cited references provides motivation to modify the solutions generally disclosed therein, in order to achieve a storage stable methylphenidate solution that includes less than about 50% water.

8. Additionally, both of the cited references fail to recognize the added benefit of including a given concentration (e.g., from about 0.5 mg/ml to about 5.0 mg/ml)of an organic acid (e.g., citric acid) in the methylphenidate solution, in order to further stabilize the solution. Although Epstein et al. list citric acid as a metal chelating agent, they fail to recognize the use of citric acid, or any organic acid, as a stabilizing agent. Thus, there is also no recognition to use an organic acid in the recited amounts.

9. In view of the foregoing, the Midha et al. and Epstein et al. references do not disclose or suggest preparing a storage stable solution of methylphenidate using a solvent system comprising a combination of less than 50% water and greater than about 50% of a non-aqueous solvent. They also do not disclose or suggest such a solution that additionally includes a given concentration of at least one organic acid, as required by the claims of the present application.

10. I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. 1001, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Clifford J. Herman

2/5/08
Date